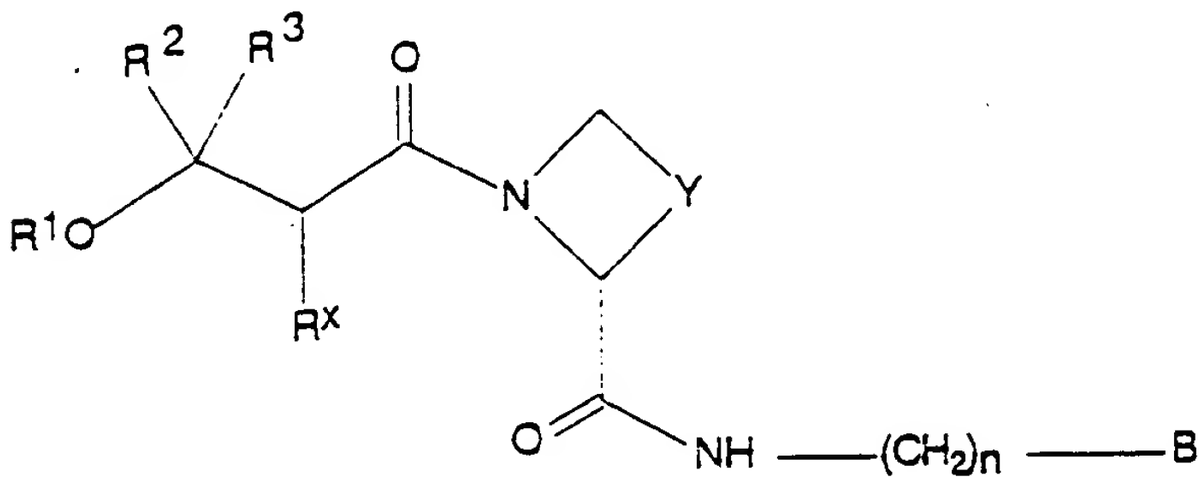
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

1. (Twice Amended) A compound of formula I,



I

wherein

R^1 represents H, $C(O)R^{11}$, $SiR^{12}R^{13}R^{14}$ or C_{1-6} alkyl which latter group is optionally substituted or terminated by one or more substituent selected from the group consisting of OR^{15} [or] and $(CH_2)_qR^{16}$;

R^{12}, R^{13} and R^{14} independently represent H, phenyl or C_{1-6} alkyl;

R^{16} represents C_{1-4} alkyl, phenyl, OH, $C(O)OR^{17}$ or $C(O)N(H)R^{18}$;

R^{18} represents H, C_{1-4} alkyl or $CH_2C(O)OR^{19}$;

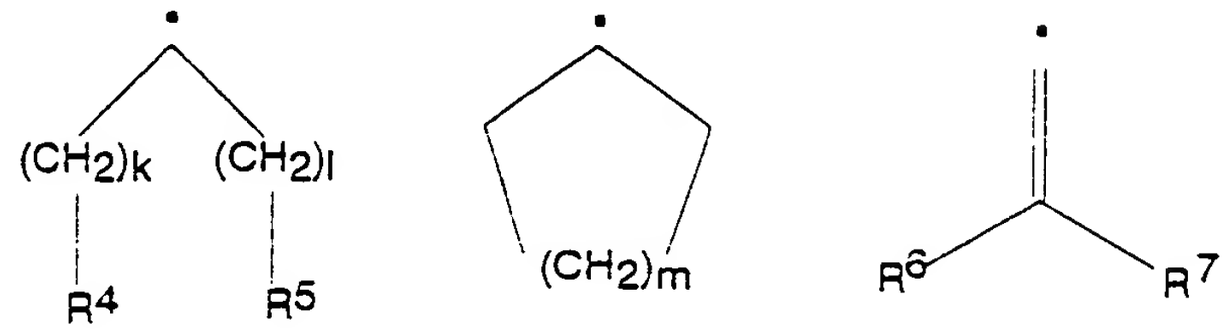
R^{15} and R^{17} independently represent H, C_{1-6} alkyl or C_{7-9} alkylphenyl;

R^{11} and R^{19} independently represent H or C_{1-4} alkyl; and

q represents 0, 1 or 2;

R^2 and R^3 [independently represent H, C_{1-4} alkyl, cyclohexyl or phenyl] are both hydrogen;

R^x represents a structural fragment of formula IIa, IIb or IIc,



IIa IIb IIc

wherein

k, l and m independently represent 0, 1, 2, 3 or 4;

R^4 and R^5 independently represent H, $Si(Me)_3$, 1- or 2-naphthyl, a polycyclic hydrocarbyl group, $CHR^{41}R^{42}$ or C_{1-4} alkyl (which latter group is optionally substituted by one or more fluorine atoms), or C_{3-8} cycloalkyl, phenyl, methylenedioxyphenyl, benzodioxanyl, benzofuranyl, dihydrobenzofuranyl, benzothiazolyl, benzoxazolyl, benzimidazolyl, coumaranonyl, coumarinyl or dihydrocoumarinyl (which latter twelve groups are optionally substituted by one or more of C_{1-4} alkyl (which latter group is optionally substituted by one or more halo substituent), C_{1-4} alkoxy, halo, hydroxy, cyano, nitro, SO_2NH_2, C(O)OH or $N(H)R^{43}$);

R^{41} and R^{42} independently represent cyclohexyl or phenyl;

R^6 and R^7 independently represent H, C_{1-4} alkyl, C_{3-8} cycloalkyl, phenyl (which latter group is are optionally substituted by one or more of C_{1-4} alkyl (which latter group is optionally substituted by one or more halo substituent), C_{1-4} alkoxy, halo, hydroxy, cyano, nitro, SO_2NH_2, C(O)OH or $N(H)R^{44}$) or together with the carbon atom to which they are attached form a C_{3-8} cycloalkyl ring;

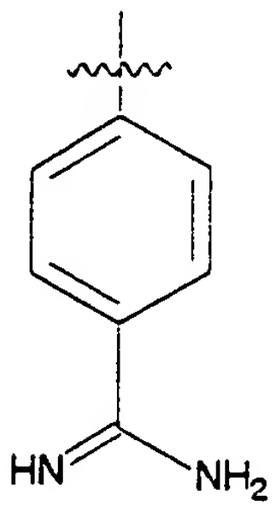
R^{43} and R^{44} independently represent H or $C(O)R^{45}$; and

R^{45} represents H, C_{1-4} alkyl or C_{1-4} alkoxy;

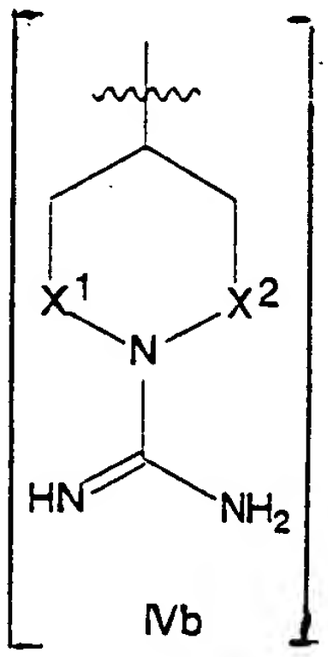
Y represents $(CH_2)_2$, CH=CH, $(CH_2)_3$, $CH_2CH=CH$ or $CH=CHCH_2$, which latter three groups are optionally substituted by C_{1-4} alkyl, methylene, oxo or hydroxy;

n represents 0, 1, 2, 3 or 4; and

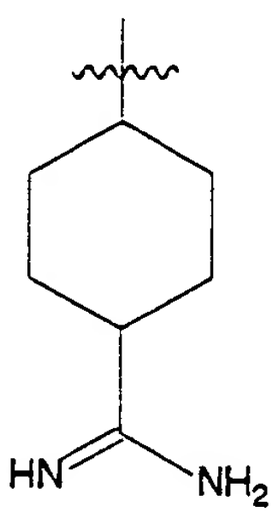
B represents a structural fragment of formula IVa[, IVb] or IVc



IVa



IVb



IVc

[wherein

X^1 and X^2 independently represents a single bond or CH_2;]

or a pharmaceutically acceptable salt thereof.

8. (Twice Amended) A compound of formula I, as defined in Claim 1, wherein B represents a structural fragment of formula IVa[.].

11. (Amended) A compound of formula I, as defined in Claim 1, provided that when R^x represents a structural fragment of formula IIa, then R^4 and/or R^5 [(as appropriate)] do/does not represent phenyl substituted by halo-substituted C_{1-6} alkyl.

12. (Amended) A compound of formula I, as defined in Claim 1, provided that when R^x represents a structural fragment of formula IIa, then R^4 and/or R^5 [(as appropriate)] do/does not represent methylenedioxyphenyl, benzodioxanyl, benzofuranyl, dihydrobenzofuranyl, benzothiazolyl, benzoxazolyl, benzimidazolyl, coumaranonyl, coumarinyl or dihydrocoumarinyl.

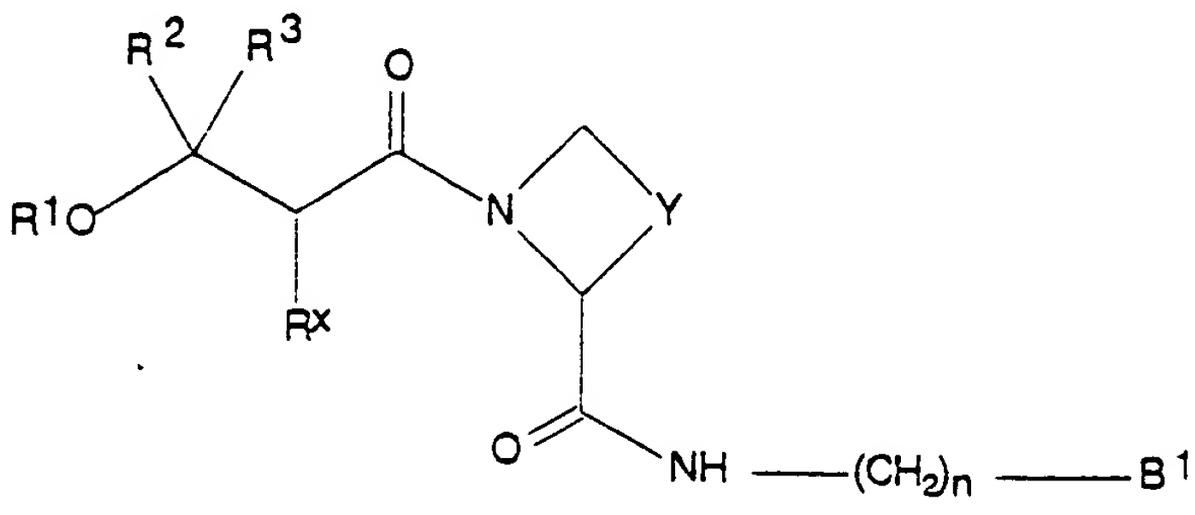
13. (Amended) A compound of formula I, as defined in Claim 1, provided that when R^x represents a structural fragment of formula IIc, then R^6 and/or R^7 [(as appropriate)] represent(s) unsubstituted phenyl.

14. (Amended) A compound of formula I, as defined in Claim 1, wherein, when R^x represents a structural fragment of formula IIa, then R^4 and/or R^5 [(as appropriate)] represent(s) phenyl substituted by halo-substituted C_{1-6} alkyl.

15. (Amended) A compound of formula I, as defined in Claim 1, wherein, when R^x represents a structural fragment of formula IIa, then R^4 and/or R^5 [(as appropriate)] represent(s) methylenedioxyphenyl, benzodioxanyl, benzofuranyl, dihydrobenzofuranyl, benzothiazolyl, benzoxazolyl, benzimidazolyl, coumaranonyl, coumarinyl or dihydrocoumarinyl.

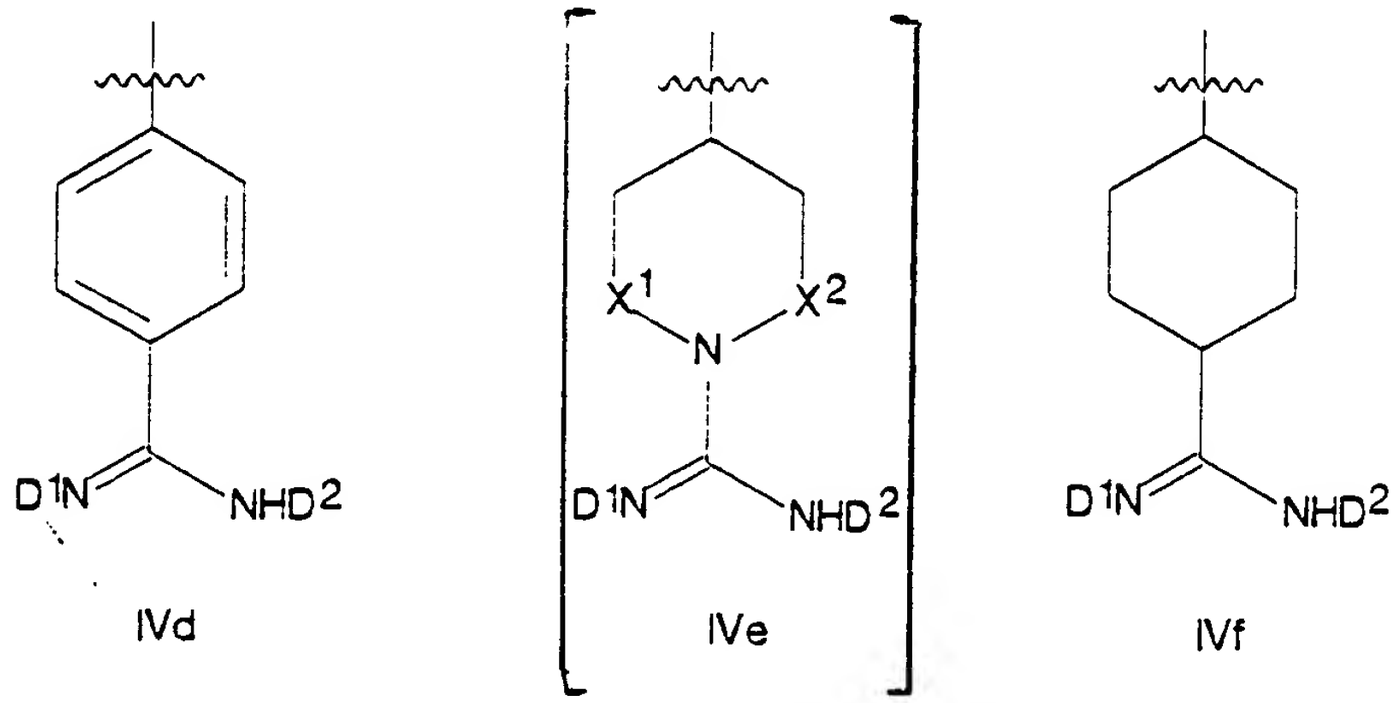
16. (Amended) A compound of formula I, as defined in Claim 1, wherein, when R^x represents a structural fragment of formula IIc, then R^6 and/or R^7 [(as appropriate)] represent(s) substituted phenyl.

17. (Amended) A compound of formula Ia,



Ia

wherein B^1 represents a structural fragment of formula IVd[, IVe] or IVf



IVd IVe IVf

wherein D^1 and D^2 independently represent H, OH, OR^a, $OC(O)R^b$, $OC(O)OR^c$, $C(O)OR^d$, or $C(O)R^e$ and R^a, R^b, R^c, R^d and R^e independently represent phenyl, benzyl, $(CH_2)_2)OC(O)CH_3$ or C_{1-6} alkyl which latter group is optionally interrupted by oxygen; and R^1, R^2, R^3, R^x, Y[, n, X^1 and X^2] and n are as defined in Claim 1, or a pharmaceutically acceptable salt thereof, provided that D^1 and D^2 do not both represent H.

20. (Twice Amended) A pharmaceutical formulation including a compound as defined in claim 1, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or [camer.] carrier.

REMARKS

Reconsideration of this application is requested. Claims 1-20, 28-30 and 32 are in the case. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "**Version With Markings To Show Changes Made**."

I. THE 35 U.S.C. 112, SECOND PARAGRAPH, REJECTION

Claims 1-10, 28-30, 32 and 33 stand rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite for the reasons stated on page 3 of the action. In response, the claims have been amended to deal with the outstanding formal points. The following comments are offered.

Claim 1 has been amended to insert the appropriate Markush language for the definition of R^1. One of the periods at the end of Claim 8 has been removed.

The Examiner has alleged that Claim 10 lacks antecedent basis in view of the definition of R^4 and R^5 allegedly not representing a "phenyl" group. This is not correct. The misunderstanding arises from the fact that a comma is missing after "C_{3-8} cycloalkyl" and before "phenyl" in the definition of R^4 and R^5. This has been corrected in the present response. This is an obvious typographical error, particularly in view of the fact that in the passage in question the phrase in

parentheses "which latter twelve groups are" would only cover 11 such groups if the phrase "C_{3-8} cycloalkyl phenyl" were construed to mean "C_{3-8} cycloalkylphenyl." Moreover, many of the examples in the present application comprise optionally substituted phenyl groups at this position.

The Examiner has objected to the expression "(as appropriate)" as found in Claims 11-16. While it is believed that no objection arises to that phraseology, Claims 11-16 have been amended to remove that language.

The Examiner asserts that Claim 17 does not further limit Claim 1 because the compounds of Claim 17 are not embraced by Claim 1. In response, Claim 17 is not intended to limit Claim 1, but rather relates to compounds of formula Ia which are protected derivatives of compounds of formula I (i.e., in place of one or other of the terminal H atoms in structural fragment B, one or other of the substituents D^1 and/or D^2 is present). This is explained at page 14, beginning at line 22 through to page 16, line 1 of the application as filed. Moreover, potential uses of the compounds of formula Ia are described at page 17, line 27 through to page 18, line 11. Since the compounds of formula Ia may be used as prodrugs of compounds of formula I, the two inventions are clearly linked by way of a common or corresponding special technical feature. No objection therefore arises with respect to Claim 17.

The Examiner has suggested that, under the definition of D^1 and D^2, an "or" is required before "$C(O)R^e$." Claim 17 has been amended to reflect that change.

Claim 20 has been amended to correct the spelling of "carrier." No new matter is entered in respect to any of the above requested changes.

Withdrawal of the outstanding 35 U.S.C. 112, second paragraph, rejection is now believed to be in order. Such action is respectfully requested.

II. DOUBLE PATENTING

Claims 1-20, 28-30, 32 and 33 stand provisionally rejected on obviousness-type double patenting grounds as allegedly unpatentable over Claims 1-18 of copending application Serial No. 09/214,143 (now U.S. patent 6,337,394; attorney docket 2257-162). This rejection is respectfully traversed. During prosecution of Serial No. 09/214,143, an obviousness-type double patenting rejection over Claims 1-24 of U.S. patent 6,255,301 (the patent which issued on the parent of the present application Serial No. 09/844,427) was successfully rebutted (see the response dated October 3, 2001 in U.S. patent 6,337,394). Clearly, therefore, obviousness-type double patenting cannot now be asserted as between the claims of the present case and the claims of U.S.

patent 6,337,394. Moreover, the PCT filing date of U.S. patent 6,337,394 is after the PCT filing date of the present case, and thus the term of the present case is shorter than that of the cited case.

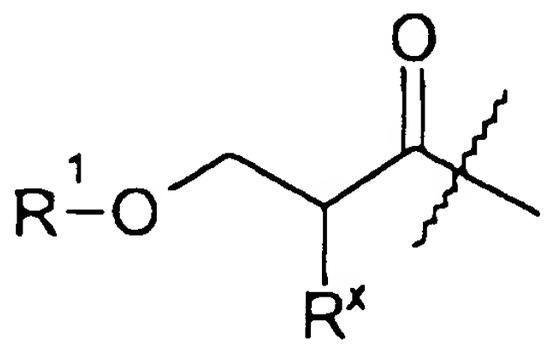
For all of the above reasons, reconsideration and withdrawal of the outstanding obviousness-type double patenting rejection are believed to be in order. Such action is respectfully requested.

III. THE OBVIOUSNESS REJECTION

Claims 1-20, 28-30, 32 and 33 stand rejected under rejected under 35 U.S.C. 103(a) as allegedly unpatentable over U.S. Patent No. 5,629,934 to Vacca et al and U.S. Patent No. 5,744,487 to Ohshima et al. That rejection is respectfully traversed.

Without conceding to the merit of the rejection, and in order to expedite prosecution, Claim 1 of the present application has been amended to incorporate the subject matter of Claim 33. Claim 33 has accordingly been canceled without prejudice. Moreover, structural fragment IVb has been deleted from the definition of B in Claim 1, and structural fragment IVe has been deleted from the definition of B in Claim 17. Claim 2 has accordingly been deleted without prejudice, and the definitional language for X^1 and X^2 has been removed from Claims 1 and 17.

The compounds as claimed in Claim 1 comprises what might be termed a β-hydroxy, β-alkoxy, β-acyloxy or β-silyloxy acid unit:



which unit is coupled to a cyclic amino acid in the manner indicated in the general formula I of Claim 1. In other words, there is a CH_2 spacer group between the carbon atom which contains R^x, and is attached to the C(O) group, and the group $-OR^1$.

Vacca contains no disclosure or suggestion of compounds not comprising a nitrogen-containing cyclic group at the right-hand side of the molecule. There is absolutely no suggestion provided by Vacca to make compounds with structural fragments IVa or IVc at this position.

With regard to Ohshima, none of the specific examples of Ohshima (and there are over 1000 of these) falls within the scope of the claims as amended.

Indeed, none comprises a CH_2 spacer group as indicated above, and there is absolutely no suggestion whatsoever in this reference, either in the generic or the specific disclosures of that document, to provide such compounds.

In light of the above, it is clear that one of ordinary skill would not have been motivated to arrive at the compounds as now claimed based on the disclosures of Vacca and Ohshima, either when taken singly or in combination. Absent any such motivation, it is clear that a *prima facie* case of obviousness has not been generated in this case. Reconsideration and withdrawal of the outstanding obviousness rejection are accordingly respectfully requested.

Allowance of the application is awaited.

Respectfully submitted,

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